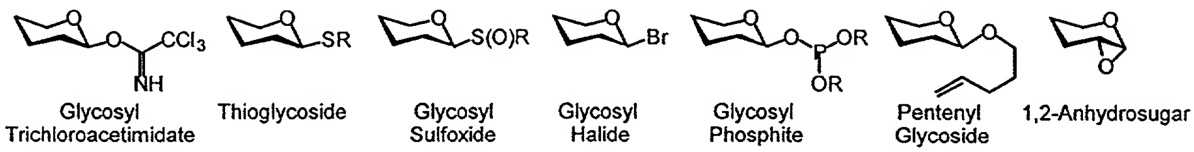


Figure 1 Commonly used glycosylating agents

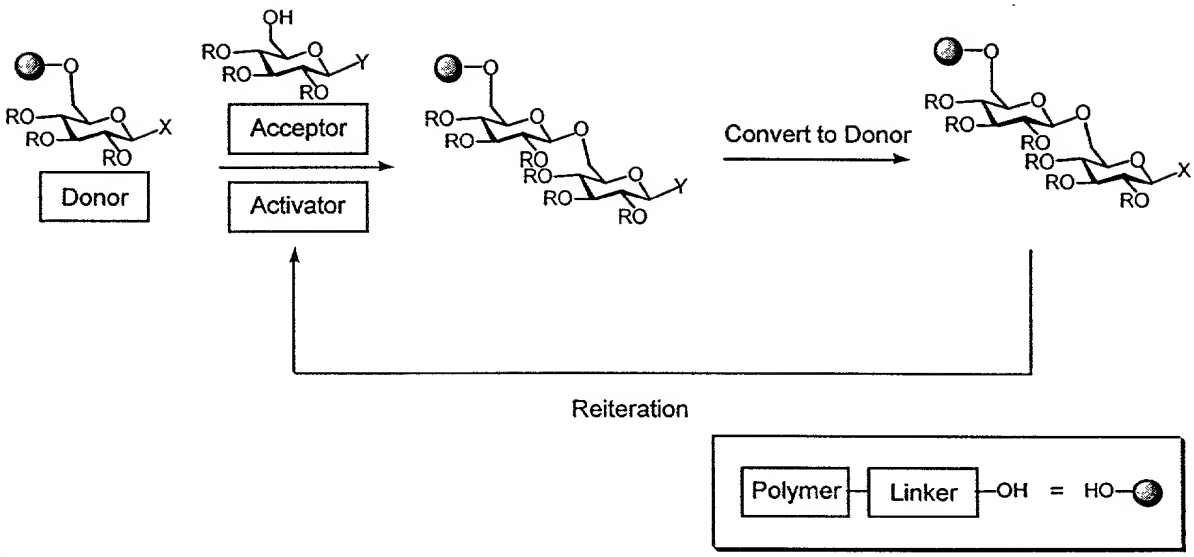


Figure 2 Donor bound solid-phase carbohydrate synthesis

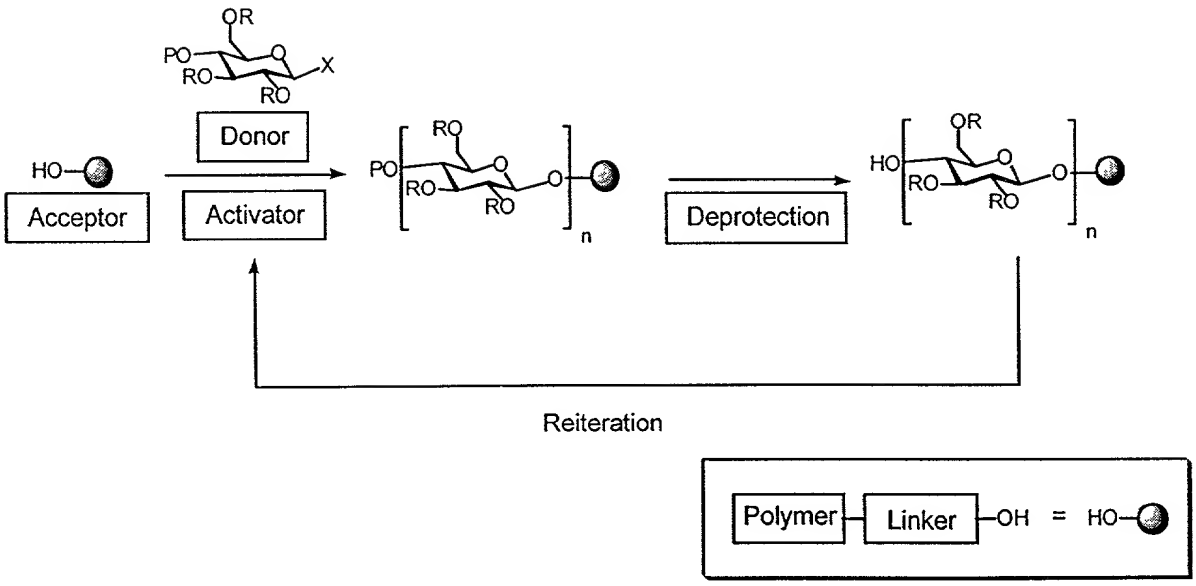
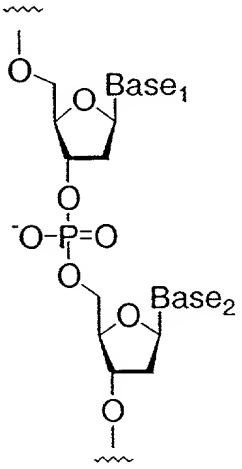


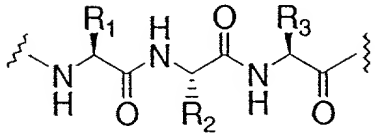
Figure 3 Acceptor bound solid-phase carbohydrate synthesis

Figure 4

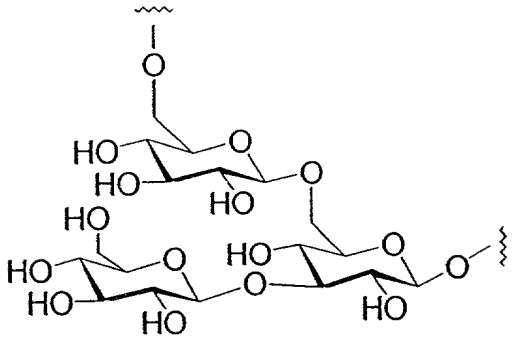
a) oligonucleotides



b) oligopeptides



c) oligosaccharides



Automated Oligosaccharide Synthesizer

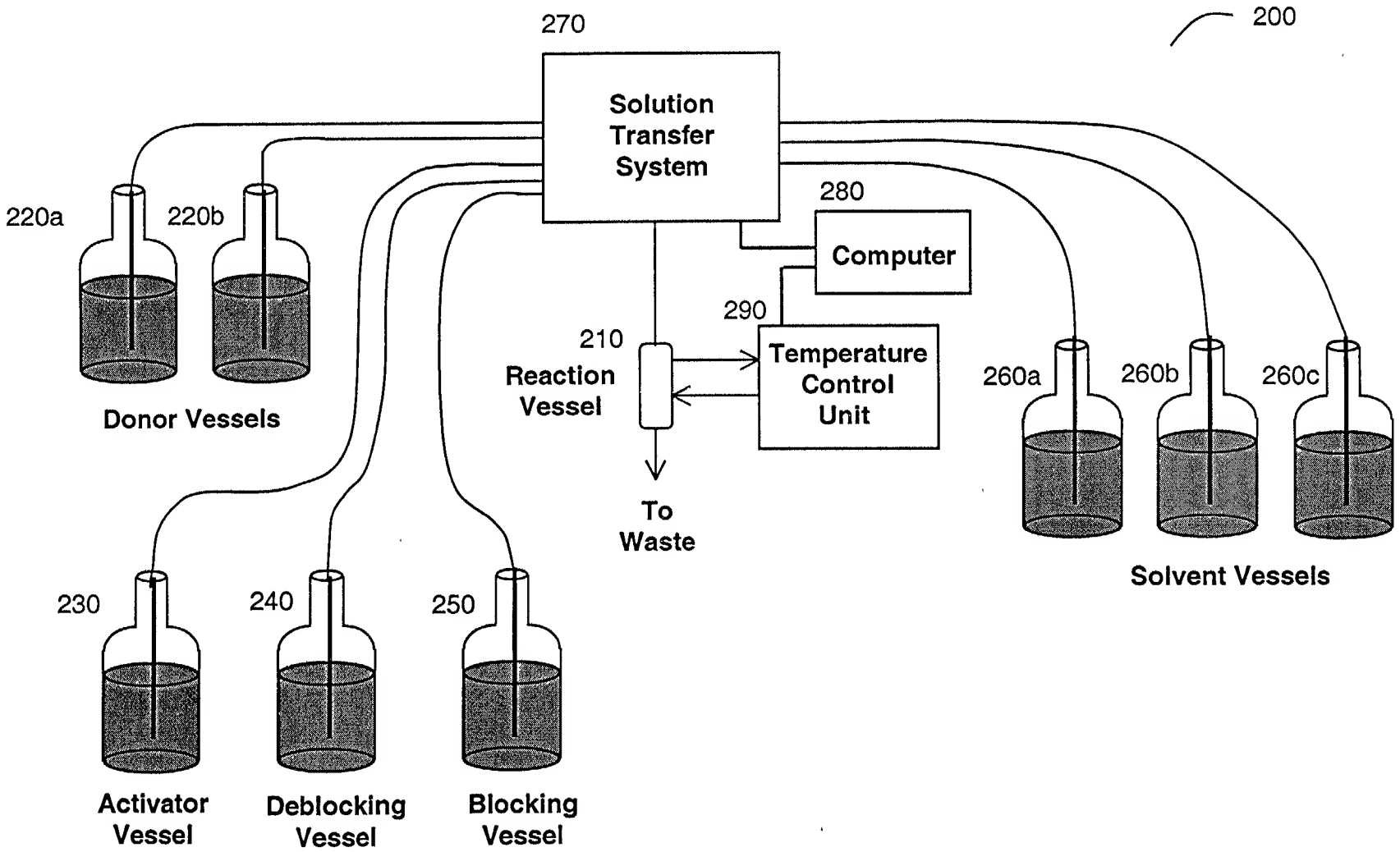


Figure 5

Automated Oligosaccharide Synthesizer

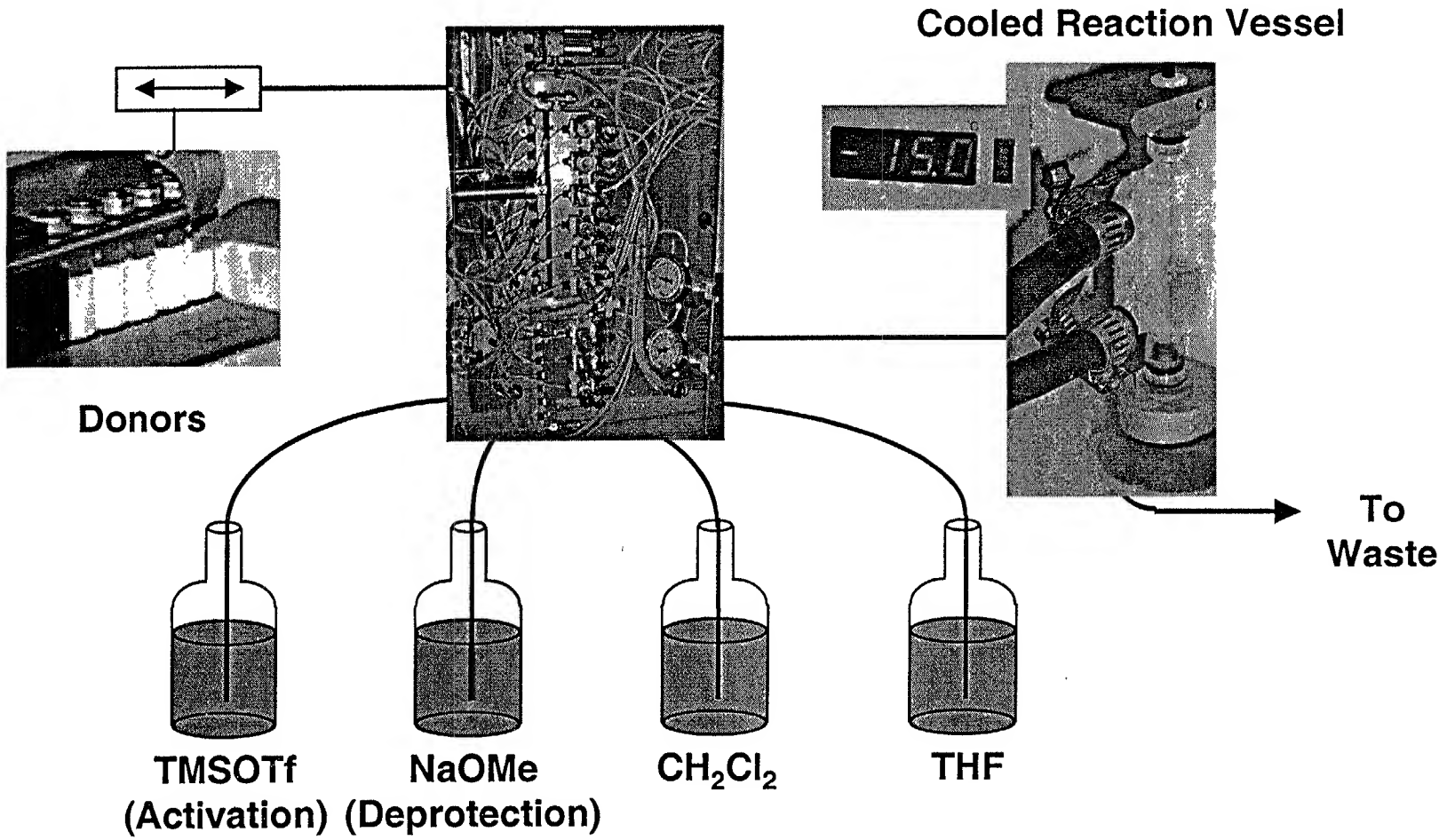


Figure 6

Double-Walled Cooled Reaction Vessel

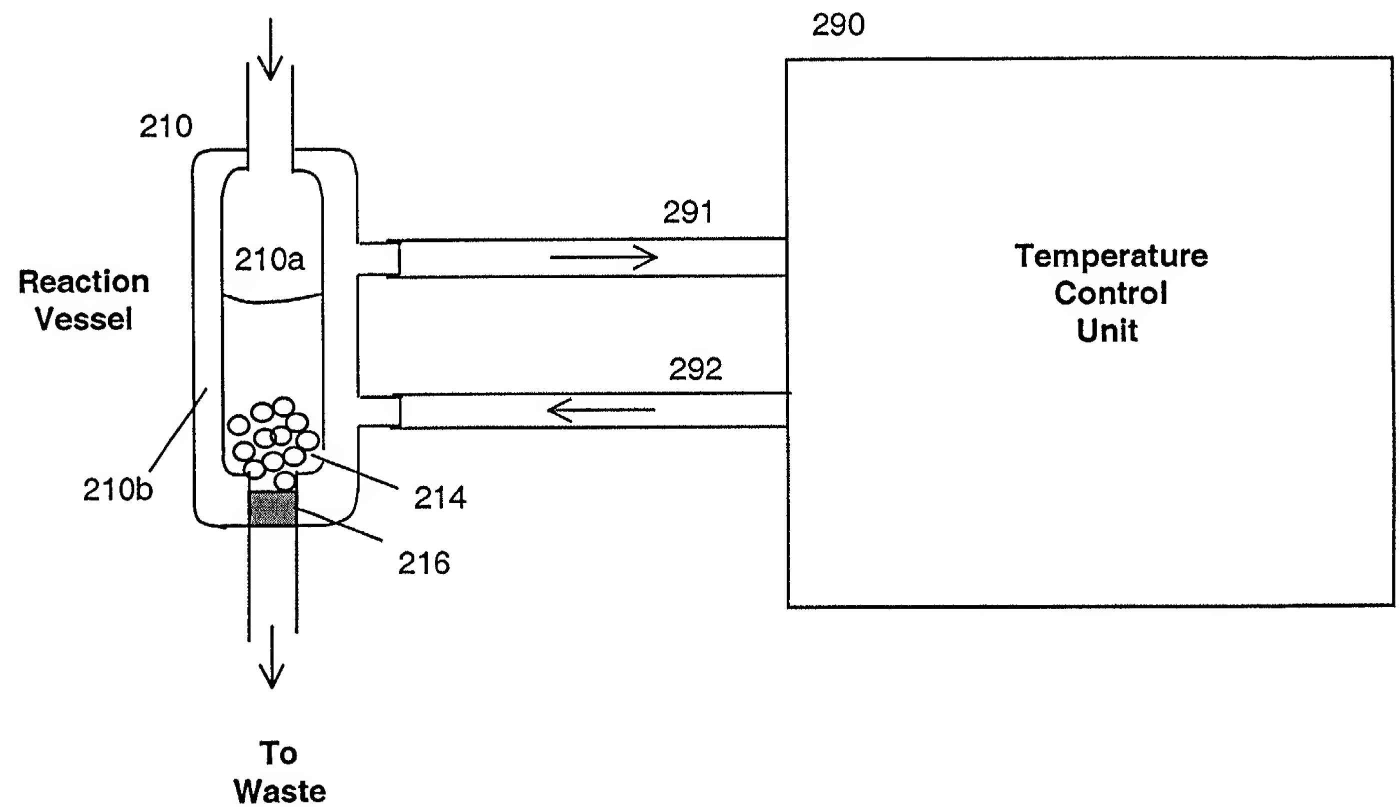
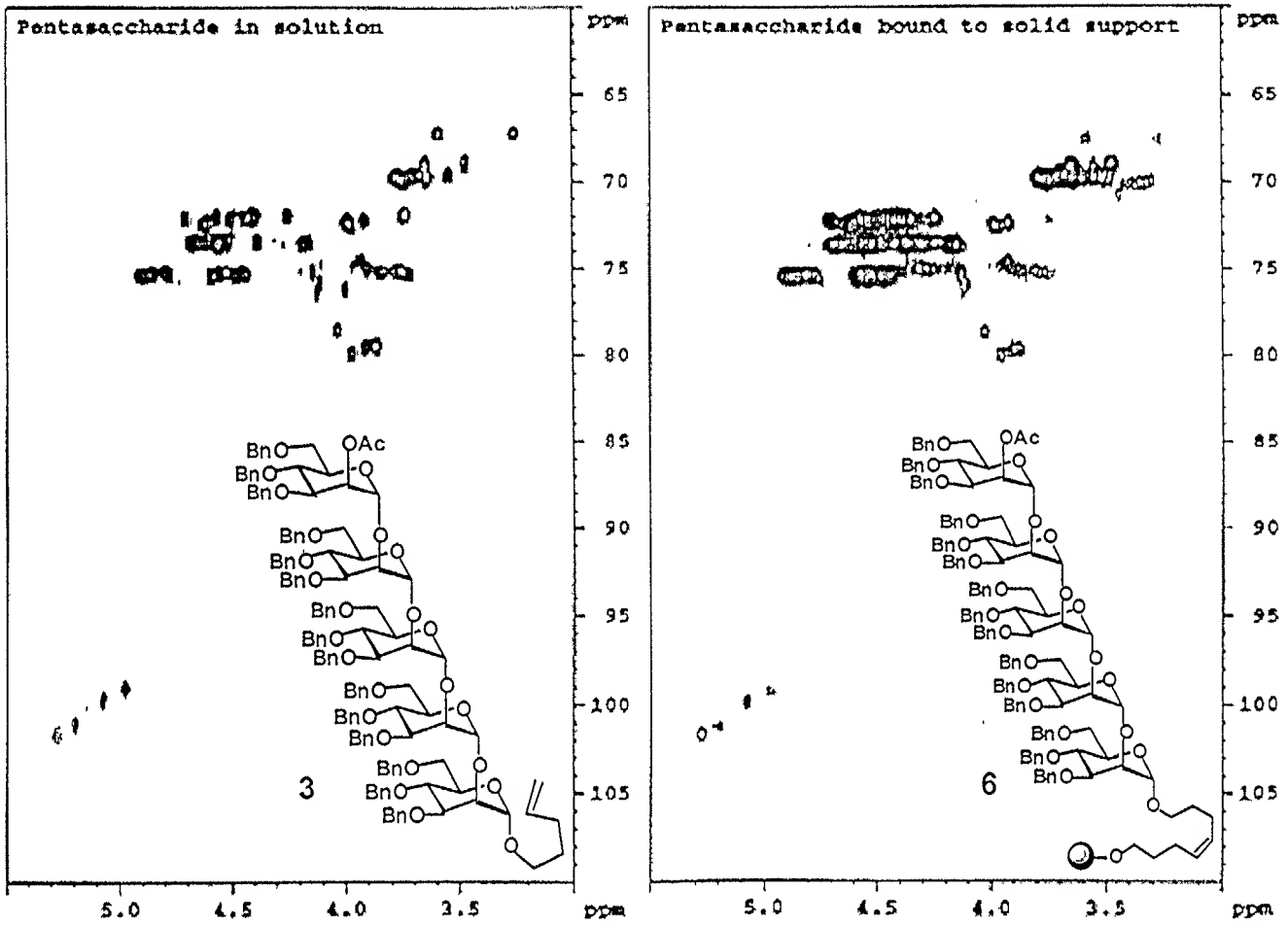


Figure 7

Figure 8

2D-NMR comparison of resin bound and solution phase pentamer



Automated Synthesis of the Phytoalexin Elicitor β-Glucan Using Glycosyl Phosphates

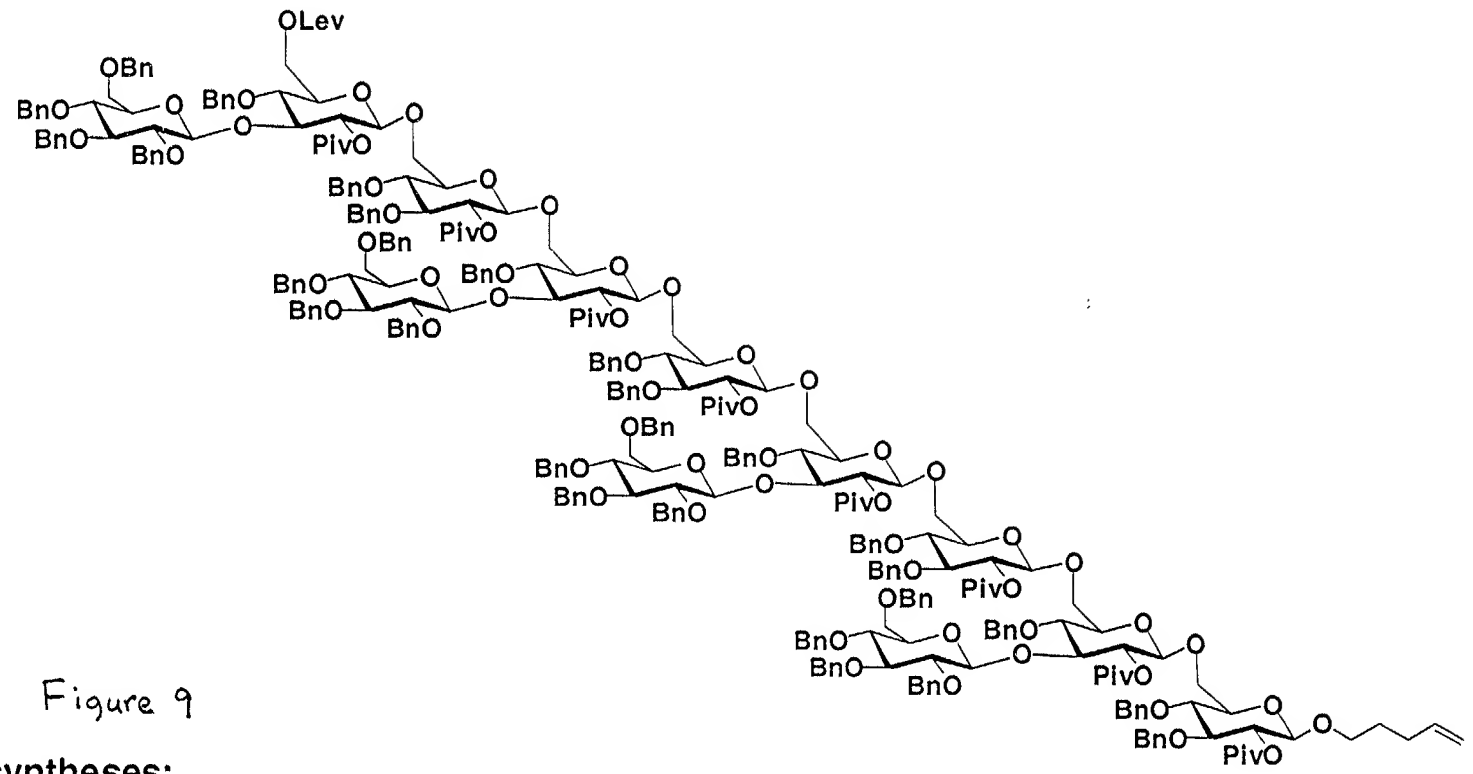


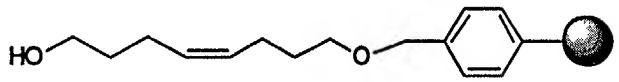
Figure 9

Prior syntheses:
Garegg et al. *Angew. Chem. Int. Ed.* 1983, *22*, 793;
van Boom et al. *Chem. Eur. J.* 1995, *1*, 16;
on soluble support: van Boom et al. *Recl. Trav. Chim. Pays-Bas* 1993, *112*, 464;
on polymer support using trisaccharide blocks: Nicolaou et al. *Angew. Chem. Int. Ed.* 1998, *37*, 1559.

Figure 10

Automated Oligosaccharide Synthesis

Chemical Issues:

- Choice of Resin (Merrifield's, Argopore, Tentagel)
- Linker: 

- Glycosylation Protocol
- Deprotection Protocol
- Capping Cycle
- Cleavage Method
- Purification Technique

Practical Issues:

- Scale (μmol-mmol)
- Cycle Development/Time
- Temperature Control Device

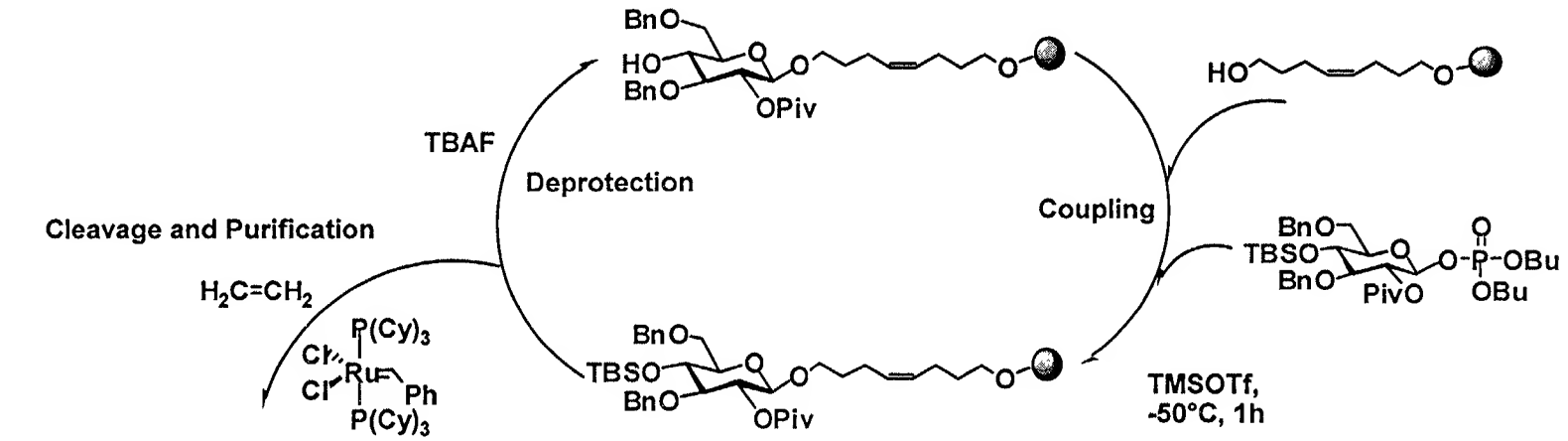
Automated Oligosaccharide Synthesis with Glycosyl Phosphates: Coupling Cycle

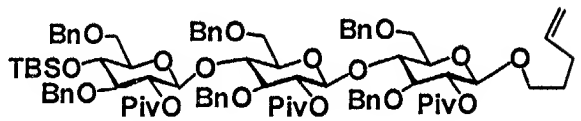
	Reagent/Solvent	Equivalents	Temperature	Time
→ Coupling	Donor	5	-15 °C	15 min
	TMSOTf	5		
Washing	CH_2Cl_2			5 min
	THF			
Coupling	Donor	5	-15 °C	15 min
	TMSOTf	5		
Washing	CH_2Cl_2			5 min
	THF			
Deprotection	N_2H_4-HOAc		15 °C	30 min
Washing	Pyr./AcOH			5 min
Deprotection	N_2H_4-HOAc		15 °C	30 min
Washing	Pyr./AcOH			5 min
		Cycle Time per residue		110 min

Figure 11

Figure 12

Solid Support Oligosaccharide Synthesis: Glycosyl Phosphate Donors





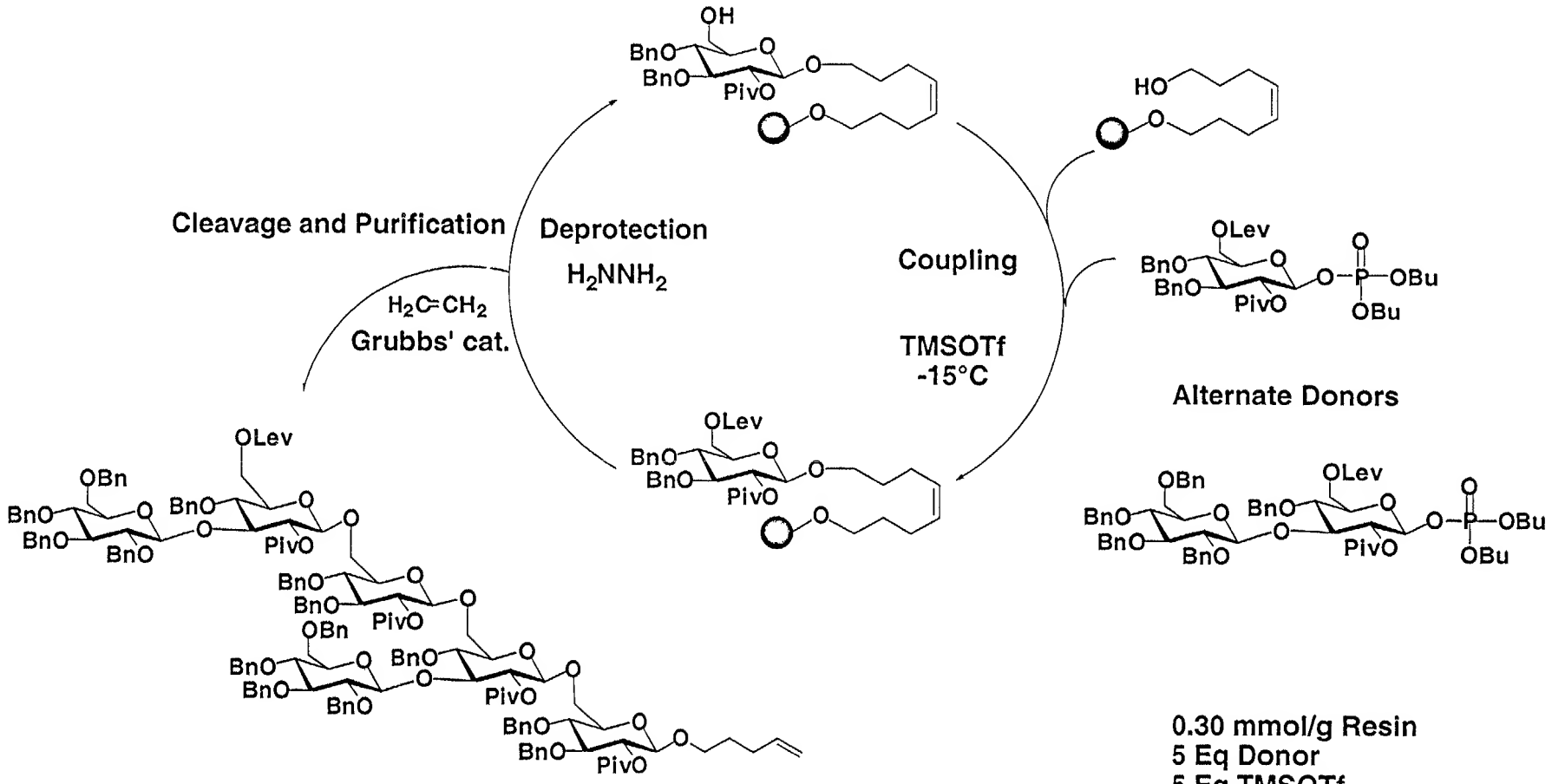
53% overall yield

Advantages:

- excess reagents drive reactions to completion
- purification only at the end of the synthesis

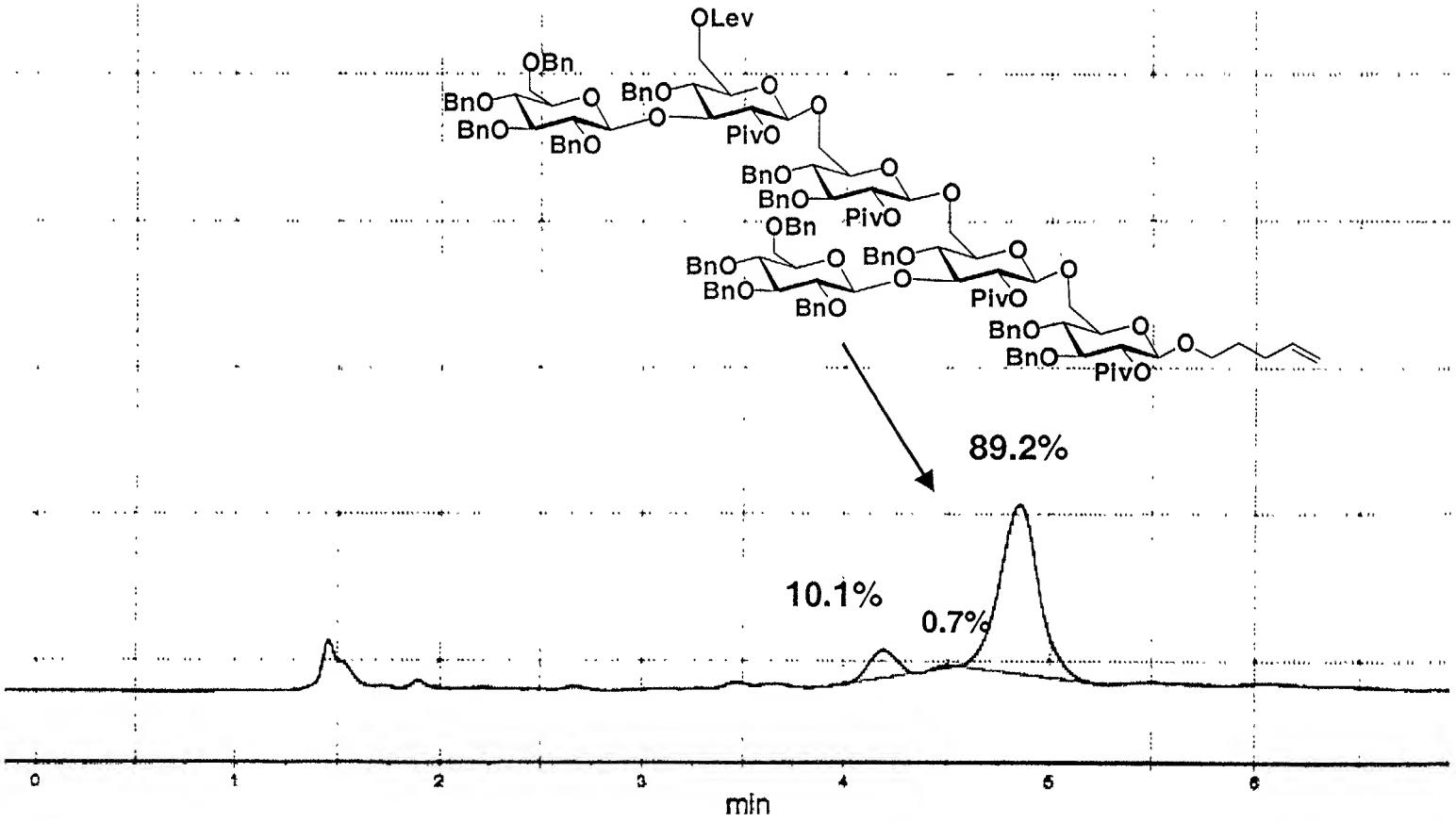
Figure 13

Automated Hexasaccharide Synthesis Using Glycosyl Phosphates



Crude HPLC Profile of the Hexamer Synthesis

Figure 14



Automated Oligomannoside Synthesis: Coupling Cycle

	Reagent/Solvent	Equivalents	Time
Coupling	Donor	10	30 min
	TMSOTf	0.5	
Washing	CH_2Cl_2		5 min
	THF		
Coupling	Donor	10	30 min
	TMSOTf	0.5	
Washing	CH_2Cl_2		5 min
	THF		
Deprotection	NaOMe		30 min
Washing	CH_2Cl_2		5 min
	THF		
Deprotection	NaOMe		30 min
Washing	CH_2Cl_2		5 min
	THF		
25μmol Scale	Cycle Time per residue		140 min

Figure 15

Solid-Phase Oligosaccharide Synthesis: Coupling Cycle Development

Figure 16

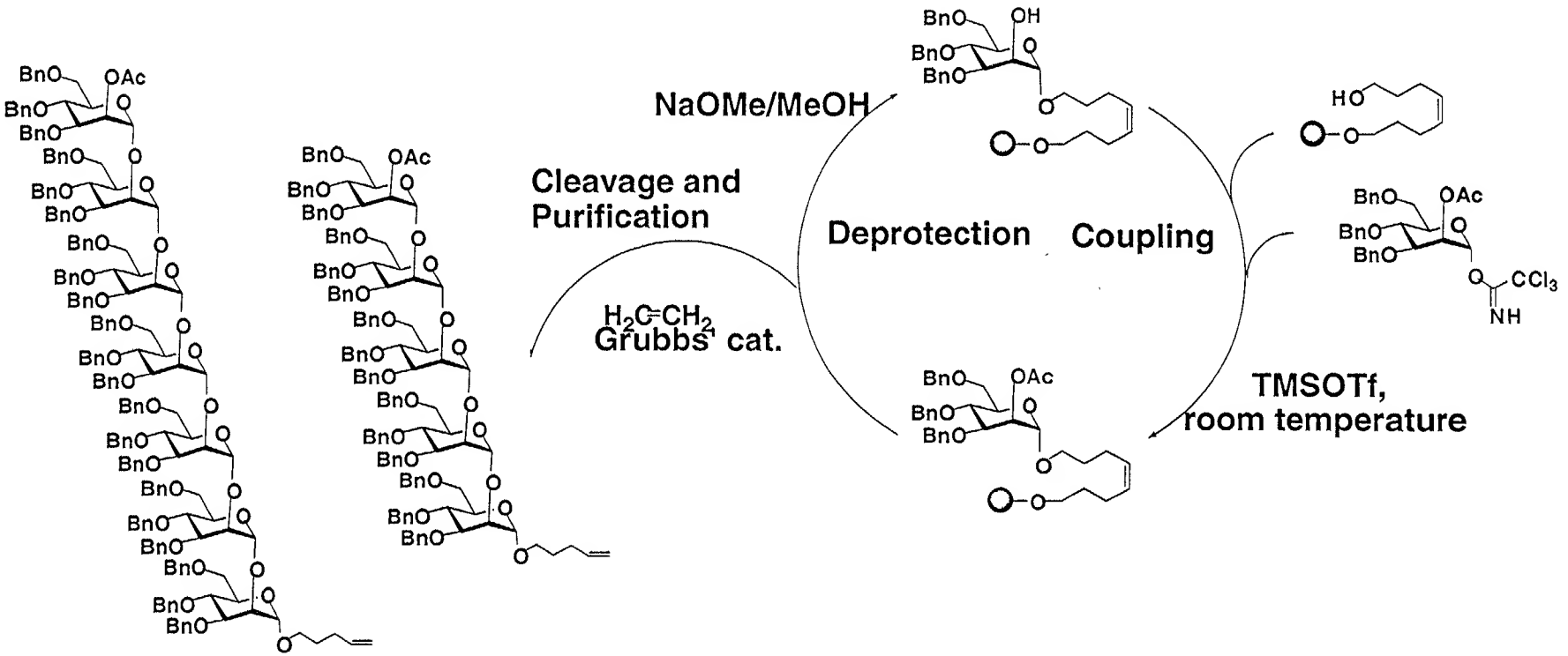


Figure 17

HR-MAS HMQC-Analysis of Pentamannosides

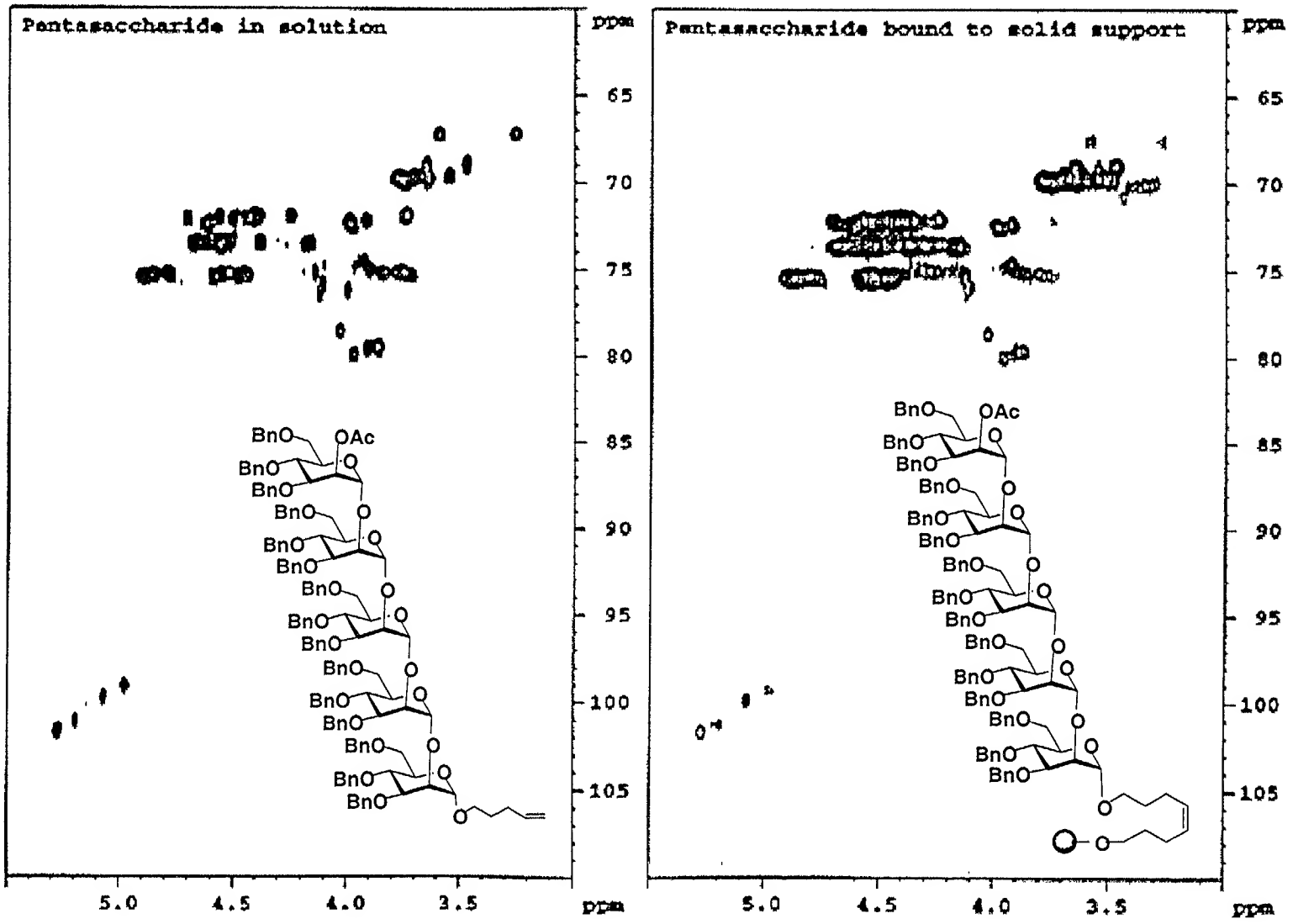
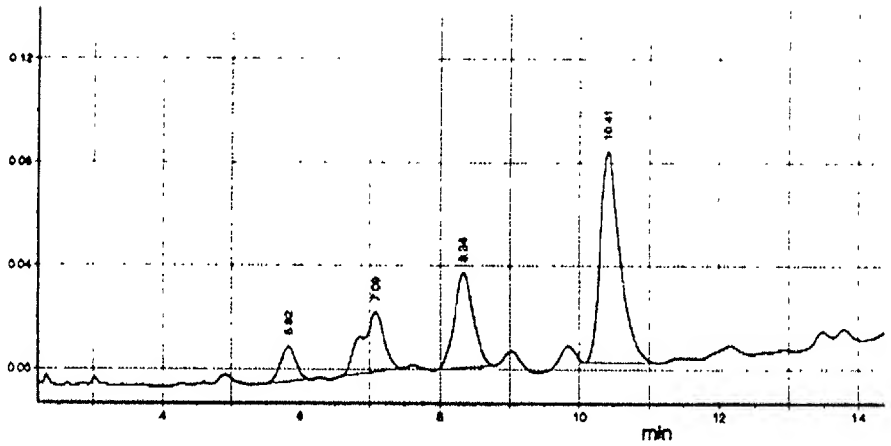
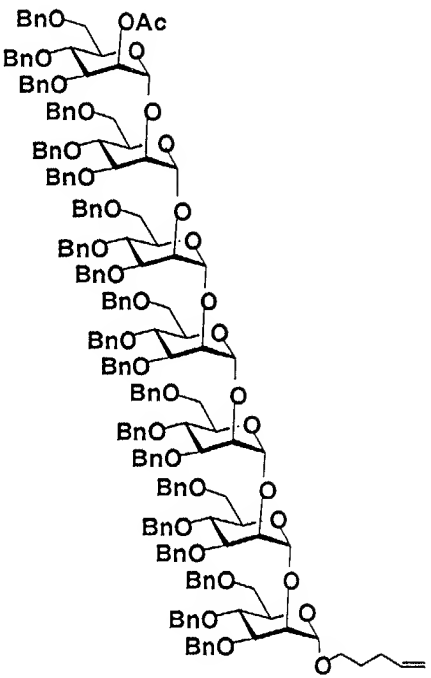


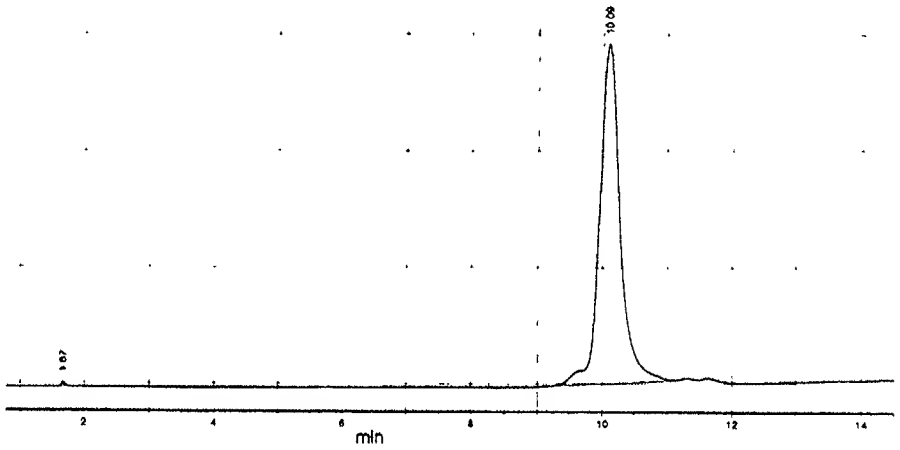
Figure 18

HPLC Purification of the Heptamannoside



Crude





Pure

42% Yield

Figure 19

Automated Synthesis of a Decamannoside Using Trichloroacetimidates

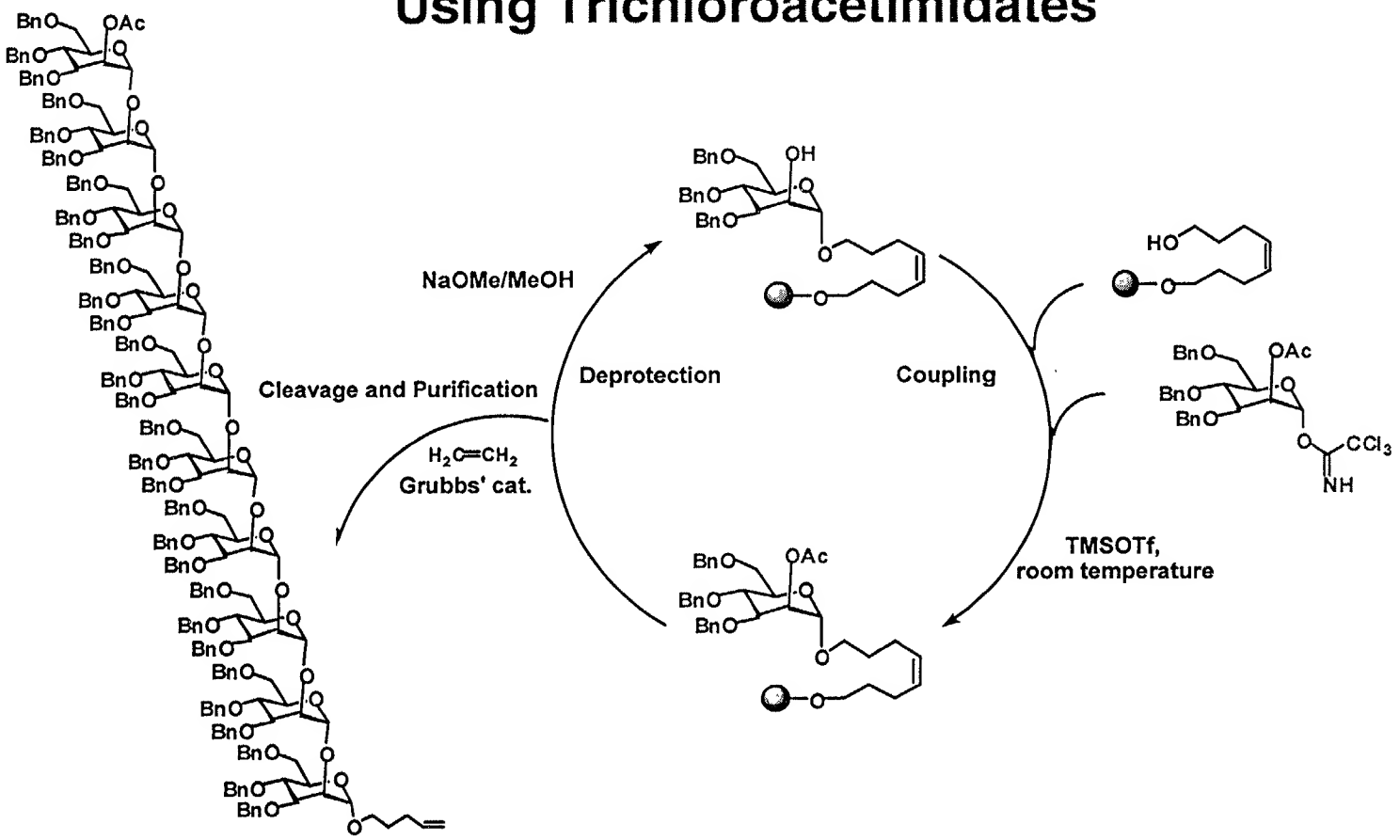


Figure 20

Automated Synthesis of Leishmania Cap Tetrasaccharide

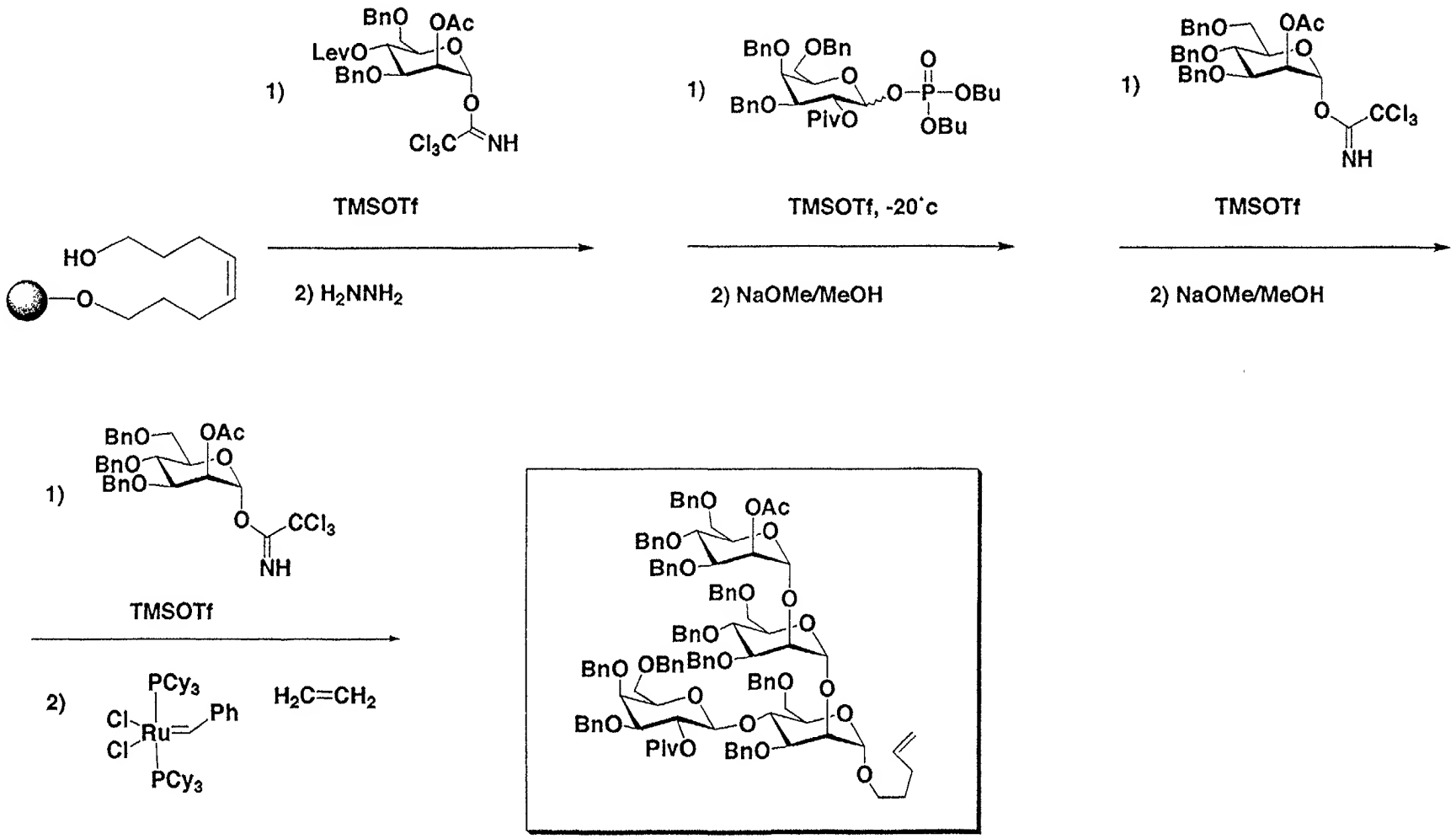
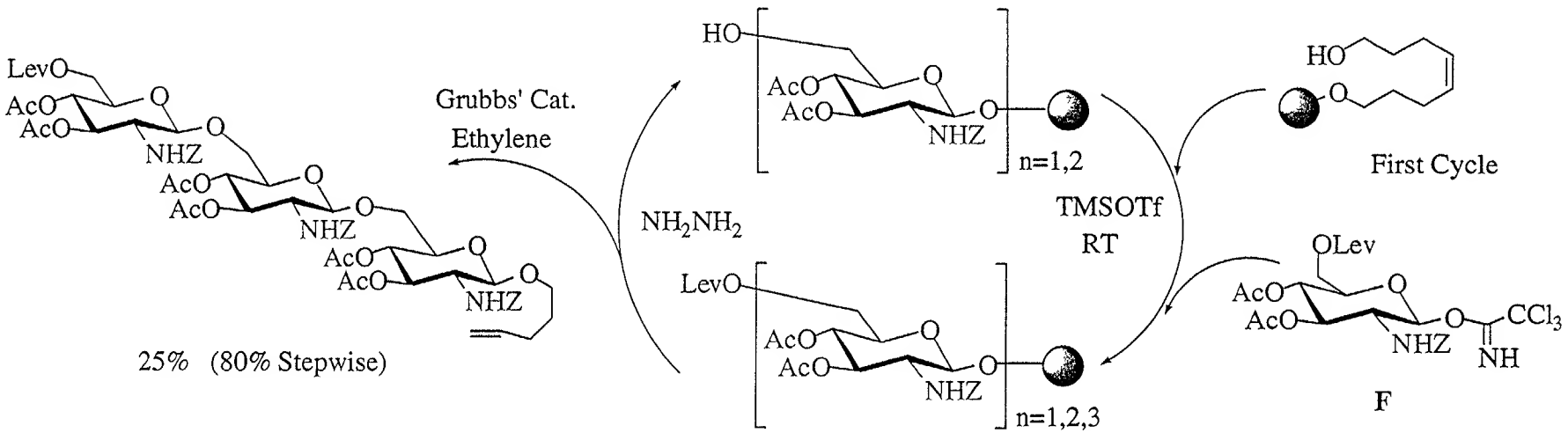


Figure 21

Automated Synthesis of GlcA Trisaccharide



Cycle:

Time: 8.5 h

Donor: 5.0 eq

Activator: 0.5 eq TMSOTf

Deprotection: 0.5 M $NH_2NH_2 \bullet H_2O$

Figure 22

Automated Synthesis of polyglucosamines